REMARKS

Claims 1, 2, 7-13, and 39-41 remain in the present application. Claims 3-6 and 14-38 have been withdrawn from consideration by the Examiner as being drawn to non-elected inventions. Claims 1, 2, 7, 9, 39, 40, and 41 are in independent form.

The Office Action sets forth an objection to the specification because of several informalities. Applicants have amended the specification in accordance with suggestions set forth in the Office Action. Reconsideration of the objection is respectfully requested.

Claim 41 is objected to because it is dependent upon non-elected claims 14 and 16. Applicants have amended claim 41 to remove any dependency upon claims 14 and 16. Claim 11 has also been objected to because "KLh" should be "KLH." Applicants have amended claim 11 accordingly. Reconsideration of these objections is respectfully requested.

As set forth in the Office Action, claims 1, 2, 7-13, and 39-41 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Office Action holds that the specification does not reasonably provide a written description about the structure associated with a function of any peptide, any fusion protein, any pharmaceutical composition, and any fragment thereof because the terms "comprising," "having," or "has" are open-ended. According to the Office Action, the peptide or fragment thereof is expanded to include additional amino acid residues at either or both ends of SEQ ID NO: 4. "Given the indefinite number of undisclosed amino acids that can be added to the peptide or fragment thereof, there is insufficient written description about the structure associated with function of any undisclosed peptide for treating any IgE disorders." (See, page 4, paragraph 3 of the Office Action).

In response thereto, Applicants have amended the claims by limiting the amino acid sequence to "consist of" SEQ ID NO: 4. As a result of the closed language directed towards the sequence, the written description requirement has been overcome. Reconsideration of the rejection is respectfully requested.

Claims 2 and 40 also stand rejected as having insufficient written description about the structure associated with function of any fusion protein because the fusion partner, i.e., the heterologous carrier protein, is not recited in the claims. In accordance with the suggestion set forth in the Office Action, the claims have been amended to include recitation of "a heterologous carrier protein." As a result of the amendments, reconsideration of the rejection is respectfully requested.

According to the Office Action, claims 1, 2, 7, 8, 10, 12, 13, and 39-40 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,629,415 (hereinafter, "the '415 patent"). According to the Office Action, "the '415 patent teaches an isolating antigenic peptide such as canine immunoglobulin E protein or fragment thereof which is useful for preparing anti-IgE immune response such as anti-IgE antibody..." (See, page 5, paragraph 5 of the Office Action). The Office Action holds that the "reference pharmaceutical composition such as canine IgE polypeptide or fragment thereof inherently does not cause anaphylaxis when administered to an animal because the reference composition is used as vaccines to treat IgE mediated-hypersensitivity response by inducing the production of anti-IgE antibodies for passive treatment of IgE hypersensitivity where the reference anti-IgE antibodies bind to soluble IgE to prevent IgE from binding to its high affinity receptors on mast cells and basophils and the reference anti-IgE antibodies do not cross-link receptor bound IgE." (See, page 5, paragraph 5 to page 6, paragraph 1 of the Office Action). (Emphasis added).

In any anticipation rejection, a comparison of the construed claim to the prior art must be performed. "To be anticipating, a prior art reference must disclose each and every limitation of the claimed invention..." In Re: Paulsen, 30 F3d 1475, 1478-79 (Fed. Cir. 1994) (*see also*, Brown v. 3M, 264 F3d 1349 (Fed. Cir. 2001) ("[T]o anticipate, every element and limitation of the claimed invention

must be found in a single prior art reference, arranged as in the claim."). According to the Office Action, the '415 patent only discloses canine IgE polypeptide or fragment thereof that inherently does not cause anaphylaxis. At no point in the '415 patent is it explicitly disclosed that the canine IgE polypeptide or fragment thereof does not cause anaphylaxis, which limitation is set forth in the claims of the present application. Hence, as a matter of law, the anticipation rejection set forth in the Office Action fails to meet the requirement set forth in well-established case law. Reconsideration of the rejection is respectfully requested.

Even if it is deemed that the claims are still anticipated by the '415 patent, Applicants have amended the claims by limiting them to the specific antigenic peptide of SEQ ID NO: 4 without prejudice. Reconsideration of the rejection is respectfully requested.

Claims 7, 9, 12, and 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,653,980 (hereinafter "the '980 patent"). According to the Office Action, the '980 patent teaches a vaccine that is a pharmaceutical composition for inducing an anti-IgE antibody immune response that does not cause anaphylaxis comprising one or more antigenic peptides such as CH2-CH3 domains from rat or human having an amino acid sequence comprising amino acid residues of a CH3 domain of an IgE molecule. (See, page 6, paragraph 3 of the Office Action).

In contradistinction, the presently claimed invention is patentably distinct over the proposed anti-IgE vaccine compositions of the '980 patent, which are based on fusion of full-length CH2-CH3 domains to a foreign carrier protein. Specifically, the antibodies induced by the anti-IgE vaccine compositions disclosed in the '980 patent result in anaphylaxis since antibodies against some portions of the CH2 and CH3 domains of the IgE molecule have been shown to cross-link the IgE receptor on the surface of mast cells and basophils and lead to production of mediators of anaphylaxis (see, Stadler, et al., Int. Arch. Allergy and Immunology, 102:121-126 (1993)). The presently claimed invention induces the production of anti-IgE antibodies, while preventing IgE from binding to its high affinity receptors on

mast cells and basophils and preventing cross-linking of receptor-bound IgE. As a result, anaphylaxis is prevented. Since the present claims at issue claim a pharmaceutical composition that does not cause anaphylaxis, the presently pending claims are patentable over the cited prior art reference. Reconsideration of the rejection is respectfully requested.

Various claims of the present application have been rejected under 35 U.S.C. § 103(a) as being unpatentable over or in view of the '415 patent and the '980 patent. As discussed above, the present claims are patentable over both the '415 and '980 patents alone, or in combination. Hence, the rejections based on 35 U.S.C. § 103(a) have been rendered moot. Reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon at least one of the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and preceding remarks, reconsideration of the rejections set forth in the Office Action and advancement of the case to issue are respectfully requested. If any remaining issues exist, Applicants request to be contacted by telephone.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on October 30, 2002.

Connie Herty

Connie Herty

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 8, lines 26-27:

The antigenic peptides can be supplied by direct administration or indirectly as "[']pro-drugs[']" using somatic cell gene therapy.

Page 13, lines 1-11:

The antigenic peptides of the present invention comprise an amino acid sequence of the CH3 domain of an IgE molecule or a fragment thereof and induce the production of anti-IgE antibodies, which are not anaphylactic. The present invention also encompasses antigenic peptides comprising an amino acid sequence of the junction of the CH3 and CH4 domains of an IgE molecule, which induce anti-IgE antibodies that are not anaphylactic. In particular, the antigenic peptides of the present invention induce the production of anti-IgE antibodies which bind to soluble (free) IgE in serum and other bodily fluids, prevent IgE from binding to its high affinity receptors on mast cells and basophils, and do not cross-link receptor-bound IgE. The antigenic peptides of the present invention may be coupled to one or more heterologous peptides. The antigenic peptides of the invention can be supplied by direct administration or indirectly as "[']pro-drugs[']" using somatic cell gene therapy.

Page 14, lines 19-33:

For example, one or more mutations at the nucleotide level which result in one or more amino acid mutations can be introduced by site-directed mutagenesis or PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "[']conservative amino acid substitution[']" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of

amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of [ ]the coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for their ability to induce anti-IgE antibodies which do not cause anaphylaxis.

Page 20, lines 29-37 and Page 21, lines 1-10:

Expression vectors containing gene inserts can be identified by three general approaches: (a) nucleic acid hybridization; (b) presence or absence of "["]marker["]" gene functions; and (c) expression of inserted sequences. In the first approach, the presence of antigenic peptide-encoding polynucleotides or antigenic fusion protein-encoding polynucleotides inserted in an expression vector(s) can be detected by nucleic acid hybridization using probes comprising sequences that are homologous to the inserted polynucleotide sequence. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "["]marker["]" gene functions (e.g., thymidine kinase activity, resistance to antibiotics, transformation phenotype, occlusion body formation in baculovirus, etc.) caused by the insertion of the gene(s) in the vector(s). For example, if a nucleic acid molecule encoding an antigenic peptide or an antigenic fusion protein is inserted within the marker gene sequence of the vector, recombinants containing the nucleic acid molecule encoding the antigenic peptide or the antigenic fusion protein insert can be identified by the absence of the marker gene function. In the third approach, recombinant expression vectors can be identified by assaying the gene product expressed by the recombinant. Such

assays can be based, for example, on the physical or functional properties of an antigenic peptide or an antigenic fusion protein in *in vitro* assay systems, e.g., binding of an antigenic peptide or an antigenic fusion protein with an anti-IgE antibody.

Page 21, lines 19-23:

The term "[']host cell["]" as used herein refers not only to the particular subject cell into which a recombinant DNA molecule is introduced but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

Page 21, lines 24-35:

A host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus, expression of the genetically engineered may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation of proteins). Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product. Expression in yeast will produce a glycosylated product. Expression in mammalian cells can be used to ensure "[']native["]" glycosylation of an antigenic peptide or antigenic fusion protein of the invention. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

Page 27, lines 1-17:

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the MaxBat.RTM. kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "["]transformed."["]

Alternatively, an antigenic peptide of the invention or an antigenic fusion protein of the invention may also be expressed in a form which will facilitate purification. For example, an antigenic peptide may be expressed as fusion protein comprising a heterologous protein such as maltose binding protein (MBP) glutathione-S-transferase (GST) or thioredoxin (TRX) which facilitates purification. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and In Vitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope "["]Flag["]" is commercially available from Kodak (New [h]Haven, Conn.).

Page 28, lines 1-18:

An antigenic peptide or an antigenic fusion protein of the invention is "["]isolated["]" or "["]purified["]" when it is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language ["]"substantially free of cellular material["]" includes preparations of protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus,

protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of a contaminating protein. When an antigenic peptide or an antigenic fusion protein of the invention is recombinantly produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When an antigenic peptide or an antigenic fusion protein of the invention is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the antigenic peptide or the antigenic fusion protein. Accordingly, such preparations of the protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the antigenic peptide or the antigenic fusion protein.

Page 30, lines 24-37 and Page 31, lines 1-12:

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of an antigenic peptide or an antigenic fusion protein of the invention, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "["]pharmaceutically acceptable["]" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "["]carrier["]" refers to a diluent, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk,

silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or p[h]H buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "[']Remington's Pharmaceutical Sciences["]" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the antigenic peptide or the antigenic fusion protein, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

CLAIMS:

1. (Amended) An isolated antigenic peptide comprising an amino acid sequence consisting of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3,] SEQ ID NO: 4[,SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14] that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal.

2. (Amended) An isolated antigenic fusion protein comprising an amino acid sequence consisting of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3] SEQ ID NO: 4[, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14] and a heterologous carrier protein that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal.

7. (Amended) A pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis comprising one or more antigenic peptides [having] consisting of an amino acid sequence [comprising] of amino acid residues of a CH3 domain of an IgE molecule or a fragment thereof.

8. (Amended) The pharmaceutical composition of claim 7, wherein at least one antigenic peptide [has] consists of the amino acid sequence of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3,] SEQ ID NO: 4 [SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14].

9. (Amended) A pharmaceutical composition for inducing an anti-IgE immune response that does not cause anaphylaxis comprising one or more antigenic fusion proteins [having] consisting of an amino acid sequence [comprising] of amino acid residues of a CH3 domain of an IgE molecule or a fragment thereof; and a heterologous carrier protein.

10. (Amended) The pharmaceutical composition of claim 9, wherein at least one antigenic fusion protein [has] consists of the amino acid sequence of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3,] SEQ ID NO: 4[,SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14].

11. (Amended) The pharmaceutical composition of claim 9, wherein the heterologous carrier protein is selected from the group consisting of KL[h]H, PhoE, rmLT, TraT, and gD from BhV-1 virus.

39. (Amended) An isolated antigenic peptide comprising an amino acid sequence consisting of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3,] SEQ ID NO: 4[, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10; SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14] or a fragment thereof, that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal.

40. (Amended) An isolated antigenic fusion protein comprising an amino acid sequence of [SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3] SEQ ID

NO: 4[, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or SEQ ID NO: 14] or a fragment thereof and a heterologous carrier protein that induces an anti-IgE immune response that does not cause anaphylaxis when administered to an animal.

41. (Amended) A pharmaceutical kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of claim 7[,] or 9 [,14 or 16].